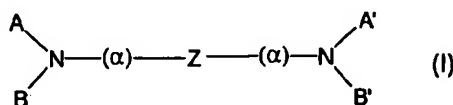


**IN THE CLAIMS:**

Amend the claims as follows.

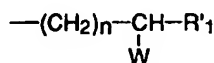
Claims 1-28. (Canceled)

29. (New) Precursors of drugs with an anti-malarial action, characterized in that they are precursors of quaternary bis-ammonium salts and that they correspond to general formula (I)



in which

- A and A' are identical to or different from one another and represent either, an A<sub>1</sub> and A'<sub>1</sub> group respectively, of formula



where n is an integer from 2 to 4; R'<sub>1</sub> represents a hydrogen atom, a C1 to C5 alkyl radical, optionally substituted by an aryl radical, a hydroxy, an alkoxy, in which the alkyl radical comprises from 1 to 5 C, or aryloxy; and W represents a halogen atom chosen from chlorine, bromine or iodine, or a nucleofuge group, *selected from the group consisting of*

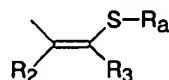
*and*  
 C<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub>, mesityl CH<sub>3</sub>-SO<sub>3</sub>, CF<sub>3</sub>-SO<sub>3</sub>, NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub> radical,

or an  $\underline{A}_2$  group which represents a formyl -CHO radical, or an acetyl -CO-CH<sub>3</sub>,

-  $\underline{B}$  and  $\underline{B}'$  are identical to or different from one another and represent

either the  $\underline{B}_1$  and  $\underline{B}'_1$  groups respectively, if  $\underline{A}$  and  $\underline{A}'$  represent  $\underline{A}_1$  and  $\underline{A}'_1$  respectively,  $\underline{B}_1$  and  $\underline{B}'_1$  representing an  $R_1$  group which has the same definition as  $\underline{R}_1$  above, but cannot be a hydrogen atom,

or the  $\underline{B}_2$  and  $\underline{B}'_2$  groups respectively, if  $\underline{A}$  and  $\underline{A}'$  represent  $\underline{A}_2$ ,  $\underline{B}_2$  or  $\underline{B}'_2$  being the  $\underline{R}_1$  group as defined above, or a group of formula

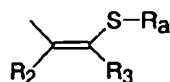


in which -R<sub>a</sub> represents an RS- or RCO- group, where  $\underline{R}$  is a linear, <sup>branched</sup> ~~branchet~~ or cyclic C1 to C6 alkyl radical, optionally substituted by one or more hydroxy, alkoxy or aryloxy group, or an amino group and/or a -COOH or COOM group, where  $\underline{M}$  is a C1 to C3 alkyl; a phenyl or benzyl radical, in which the phenyl radical is optionally substituted by at least one C1 to C5 alkyl or alkoxy radical, these being optionally substituted by an amino group, or by a nitrogenous or oxygenous heterocycle, a -COOH or -COOM group; or a saturated -CH<sub>2</sub>-heterocycle group, with 5 or 6 elements, nitrogenous and/or oxygenous;  $\underline{R}_2$  represents a hydrogen atom, a C1 to C5 alkyl radical, or a -CH<sub>2</sub>-COO-alkyl (C1 to C5) group; and  $\underline{R}_3$  represents a hydrogen atom, a C1 to C5 alkyl or alkenyl radical, optionally substituted by -OH, a phosphate group, an alkoxy radical, in which the alkyl radical is C1 to C3, or an aryloxy radical; or an alkyl (or aryl), carbonyloxy

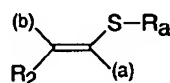
group; or also  $\underline{R}_2$  and  $\underline{R}_3$  together form a ring with 5 or 6 carbon atoms; R and  $\underline{R}_3$  can be linked to form a cycle of 5 to 7 atoms (carbon, oxygen, sulphur)

-  $\underline{\alpha}$  represents

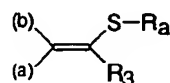
either a single bond, when  $\underline{A}$  and  $\underline{A}'$  represent  $\underline{A}_1$  and  $\underline{A}'_1$ ; or when  $\underline{A}$  and  $\underline{A}'$  represent  $\underline{A}_2$ , i.e. a -CHO or -COCH<sub>3</sub> group, and  $\underline{B}_2$  and  $\underline{B}'_2$  represent



or, when  $\underline{A}$  and  $\underline{A}'$  represent  $\underline{A}_2$  and  $\underline{B}_2$  and  $\underline{B}'_2$  represent  $\underline{R}_1$ , a group of formula



or a group of formula

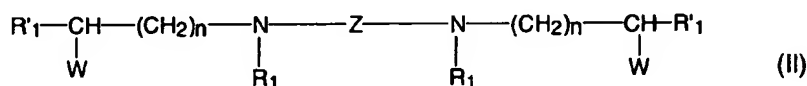


in which (a) represents a bond towards  $\underline{Z}$  and (b) a bond towards the nitrogen atom.

-  $\underline{Z}$  represents a C6 to C21 alkylene radical, optionally with insertion of one or more multiple bonds, and/or one or more O and/or S heteroatoms, and/or one or more aromatic rings, and the pharmaceutically acceptable salts of these compounds,

provided that  $R'_1$  does not represent H or a C1 or C2 alkyl radical, when  $n = 3$  or  $4$ ,  $R_1$  represents a C1 to C4 alkyl radical and Z represents a C6 to C10 alkylene radical.

<sup>2</sup>  
~~30.~~ (New) Precursors according to claim <sup>1</sup>~~29~~, characterized in that it relates to haloalkylamines, corresponding to general formula (II)



in which  $R_1$ ,  $R'_1$ ,  $W$ ,  $n$  and  $Z$  are as defined in claim 29.

<sup>3</sup>  
~~31.~~ (New) Precursors according to claim <sup>1</sup>~~29~~, wherein Z represents a C13 to C21 alkylene radical.

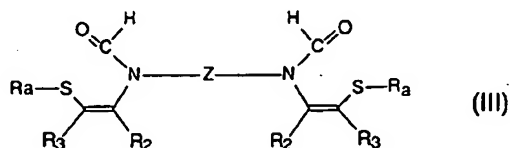
<sup>4</sup>  
~~32.~~ (New) Precursors according to claim <sup>3</sup>~~31~~, characterized in that  $Z$  represents a  $-(CH_2)_{16}$  - group.

<sup>5</sup>  
~~33.~~ (New) Precursors according to claim <sup>2</sup>~~30~~ or <sup>3</sup>~~31~~, characterized in that  $R_1$  is a methyl radical.

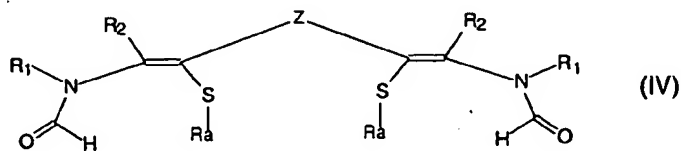
<sup>6</sup>  
~~34.~~ (New) Precursors according to claim <sup>2</sup>~~30~~, characterized in that  $R_1$  is a methyl radical and  $R'_1$  is either a hydrogen atom, or a methyl radical, and  $W$  is a chlorine atom.

3  
35. (New) Precursors according to claim 31, characterized in that they are chosen from N, N'-dimethyl-N,N'-(5-chloropentyl)-1,16-hexadecanediamine hydrochloride, or N, N'-dimethyl-N,N'-(4-chloropentyl)-1,16-hexadecanediamine hydrochloride.

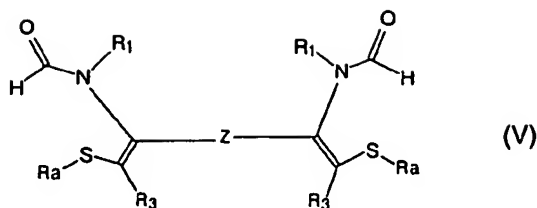
8  
36. (New) Precursors according to claim 29, characterized in that it concerns precursors of thiazolium corresponding to general formula (III).



or to general formula (IV)



or to general formula (V)



in which  $\underline{R_a}$ ,  $\underline{R_1}$ ,  $\underline{R_2}$ , and  $\underline{Z}$  are as defined in claim 29.

9  
 37. (New) Precursors according to claim 36, characterized in that they correspond to formula III in which  $\underline{R_a}$  represents an RCO- radical.

10  
 38. (New) Precursors according to claim 37, characterized in that they are chosen from N,N'-diformyl-N,N'-di[1-methyl-2-S-thiobenzoyl-4-methoxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-S-(p-diethylaminomethylphenylcarboxy)thio-4-methoxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-S-(p-morpholino-methylphenylcarboxy)-thio-4-methoxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-S-thiobenzoyl-4-methoxybut-1-enyl]-1,16-diaminohexadecane, and N,N'-diformyl-N,N'-di[1(2-oxo-4,5-dihydro-1,3-oxathian-4-ylidene)ethyl]1,12-diaminododecane.

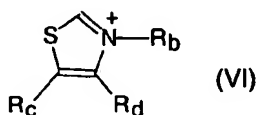
11  
 39. (New) Precursors according to claim 37, characterized in that  $\underline{R_a}$  represents RS-.

<sup>2</sup>40. (New) Precursors according to claim <sup>11</sup>39, characterized in that they are chosen from N,N'-diformyl-N,N'-di[1-methyl-2-tetrahydrofurfuryl-methyldithio-4-hydroxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-propyldithio-4-hydroxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-benzyl-dithio-4-hydroxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-(2-hydroxyethyl)-dithio-4-hydroxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-propyldithio-4-methoxybut-1-enyl]-1,12-diaminododecane, and N,N'-diformyl-N,N'-di[1-methyl-2-propyldithio-ethenyl]-1,12-diaminododecane.

<sup>3</sup>41. (New) Precursors according to claim <sup>8</sup>36, characterized in that they correspond to formula IV and are chosen from 2,17-(N,N'-diformyl-N,N'-dimethyl)diamino-3,16-S-thio-p-methoxybenzoyl-6,13-dioxaoctadeca-2,16-diene, 2,17-(N,N'-diformyl-N,N'-dibenzyl)diamino-3,16-S-thio-p-methoxybenzoyl-6,13-dioxaoctadeca-2,16-diene, ethyl 3,18 (N,N'-diformyl-N,N'-dimethyldiamino-4,17-S-thiobenzoyl-eicosa-3,17-dienedioate (TE12), ethyl 3,18-(N,N'-diformyl-N,N'-dibenzyl)diamino-4,17-S-thiobenzoyl-eicosa-3,17-dienedioate.

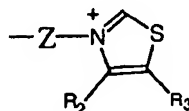
<sup>14</sup>42. (New) Precursors according to claim <sup>8</sup>36, characterized in that they correspond to formula (V) and are chosen from 2,15-(N,N'-diformyl-N,N'-dimethyl)diamino-1,16-S-thiobenzoyl-hexadeca-1,15-diene. 2,15-(N,N'-diformyl-N,N'-dibenzyl)diamino-1,16-S-thio-benzoyl-hexadeca-1,15-diene.

43. (New) The cyclized derivatives corresponding to the precursors of thiazolium of claim 29, said derivatives having general formula (VI)



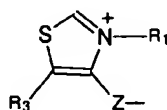
in which

R<sub>b</sub> represents R<sub>1</sub> or I, I representing the group of formula

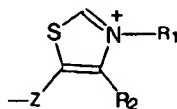


provided that Z does not represent a C6 to C8 alkylene radical, when R<sub>c</sub>, R<sub>d</sub>, R<sub>2</sub> and R<sub>3</sub> represent a methyl radical.

R<sub>d</sub> represents R<sub>2</sub> or P, P representing the group of formula



R<sub>c</sub> represents R<sub>3</sub> or U, U representing the group of formula



R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Z being as defined in claim 29,



it being understood that  $\underline{R}_b = \underline{T}$ , if  $\underline{R}_c = \underline{R}_3$  and  $\underline{R}_d = \underline{R}_2$ ;  $\underline{R}_d = \underline{P}$ , if  $\underline{R}_c = \underline{R}_3$  and  $\underline{R}_b = \underline{R}_1$ ; and  $\underline{R}_c = \underline{U}$ , if  $\underline{R}_b = \underline{R}_1$  and  $\underline{R}_d = \underline{R}_2$ .

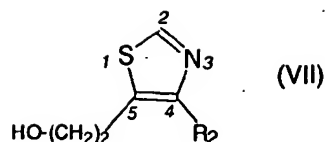
<sup>16</sup>  
~~44~~. (New) Process for obtaining precursors of thiazolium of general formula (III) to (IV) according to claim <sup>7</sup>~~35~~, characterized in that it comprises the reaction in basic medium of a thiazole derivative of formula (VI).

<sup>17</sup>  
~~45~~. (New) Process according to claim <sup>16</sup>~~44~~, characterized in that in order to obtain the compounds in which  $\underline{R}_a = \text{RCO-}$ , a derivative of thiazolium of formula (VI) is reacted with an  $\text{RCOR'}$  derivative, where  $\underline{R}$  is as defined in claim 1 and  $\underline{R'}$  is a halogen atom, and in order to obtain the compounds in which  $\underline{R}_a = \text{RS-}$ , said thiazolium derivatives of formula (VI) are reacted with a thiosulphate derivative  $\text{RS}_2\text{O}_3\text{Na}$ .

<sup>18</sup>  
~~46~~. (New) Process according to claim <sup>15</sup>~~43~~ or <sup>16</sup>~~44~~, characterized in that

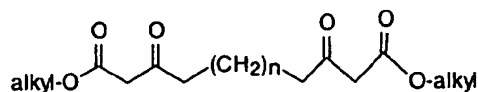
- in order to obtain the compounds of formula (III) a thiazole derivative suitably substituted with an alkyl dihalide is reacted, under reflux in an organic solvent, the opening of the thiazolium ring then takes place in basic medium, and by the action either of  $\text{R-COCl}$ , or of  $\text{RS}_2\text{O}_3\text{Na}$ ,

- in order to obtain the compounds of formula IV, which comprise an oxygen in the  $\underline{Z}$  chain, a thiazole derivative of general formula (VII)



is reacted with an alkane dihalide, in basic medium, then the addition of  $R_1X$ , the reaction medium being advantageously taken to reflux in an organic solvent, in particular alcoholic such as ethanol, for a duration sufficient to obtain the quaternization of the nitrogen atom of the thiazole by fixing  $R_1$ , the opening of the thiazolium ring then being obtained in basic medium, then by the action either of  $R-COCl$ , or of  $RS_2O_3Na$ ,

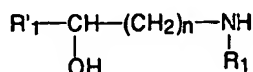
- in order to obtain the compounds of formula (IV) not comprising oxygen in the  $Z$  chain, a compound of structure



is firstly synthesized by reacting an alkyl acetoacetate with  $NaH$ , followed by alkylation, then the addition of a dihalogenoalkane, the compound obtained then being dibrominated, then thioformamide is added and, after reflux for several days,  $R_1X$ , which leads, after renewed reflux for several days, to a thiazolium, the opening of which is then carried out in basic medium, then the action of  $R-COCl$  or of  $R-S_2O_3Na$ ,

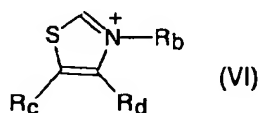
- in order to obtain the compounds of formula (V) not comprising oxygen in the  $Z$  chain, a  $Z(CO-CH_2 X)_2$  compound is reacted with  $CH(=S)NH_2$ , then  $R_1X$  is added, the opening of the thiazolium ring then being carried out in basic medium, then by adding  $R-COCl$  or  $R-S_2O_3Na$ .

47. (New) Process for obtaining haloalkylamines according to claim 29, characterized in that it comprizes the alkylation of an amino alcohol of formula



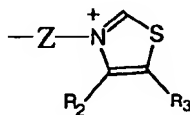
by an alkyl  $\alpha,\omega$ -dihalide X-Z-X, which leads to a bis-aminoalcohol treated with a compound capable of releasing the W group.

48. (New) Pharmaceutical compositions, characterized in that they contain an effective quantity of at least one precursor as defined in claim 29, or at least one cyclized derivative of general formula (VI):

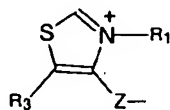


in which

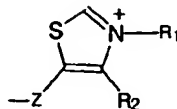
$\text{R}_b$  represents  $\text{R}_1$  or  $\text{I}$ ,  $\text{I}$  representing the group of formula:



$\text{R}_d$  represents  $\text{R}_2$  or  $\text{P}$ ,  $\text{P}$  representing the group of formula



R<sub>c</sub> represents R<sub>3</sub> or U, U representing the group of formula

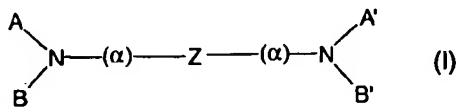


R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and Z being as defined in claim 29,

it being understood that R<sub>b</sub> = T, if R<sub>c</sub> = R<sub>3</sub> and R<sub>d</sub> = R<sub>2</sub>; R<sub>d</sub> = P, if R<sub>c</sub> = R<sub>3</sub> and R<sub>b</sub> = R<sub>1</sub>; and R<sub>c</sub> = U, if R<sub>b</sub> = R<sub>1</sub> and R<sub>d</sub> = R<sub>2</sub>.

in combination with a pharmaceutically inert vehicle.

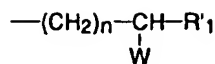
2  
 49. (New) A method of treating at least one of malaria and babesiosis comprising administering to an animal in need of said treatment a quaternary bis-ammonium salt of formula I



in which

- A and A' are identical to or different from one another and represent

either, an A<sub>1</sub> and A'<sub>1</sub> group respectively, of formula



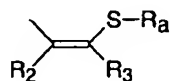
where n is an integer from 2 to 4; R<sub>1</sub>' represents a hydrogen atom, a C1 to C5 alkyl radical, optionally substituted by an aryl radical; a hydroxy, an alkoxy, in which the alkyl radical comprises from 1 to 5 C, or aryloxy; and W represents a halogen atom chosen from chlorine, bromine or iodine, or a nucleofuge group, such as the tosyl CH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub>, mesityl CH<sub>3</sub>-SO<sub>3</sub>, CF<sub>3</sub>-SO<sub>3</sub>, NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub> radical,

or an A<sub>2</sub> group which represents a formyl -CHO radical, or an acetyl-CO CH<sub>3</sub> radical,

- B and B' are identical to or different from one another and represent

either the B<sub>1</sub> and B<sub>1</sub>' groups respectively, if A and A' represent A<sub>1</sub> and A<sub>1</sub>' respectively, B<sub>1</sub> and B<sub>1</sub>' representing an R<sub>1</sub> group which has the same definition as R<sub>1</sub>' above, but cannot be a hydrogen atom,

or the B<sub>2</sub> and B<sub>2</sub>' groups respectively, if A and A' represent A<sub>2</sub>, B<sub>2</sub> or B<sub>2</sub>' being the R<sub>1</sub> group as defined above, or a group of formula

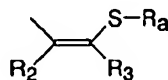


in which -R<sub>a</sub> represents an RS- or RCO- group, where R is a linear, branched or cyclic C1 to C6 alkyl radical, optionally substituted by one or more hydroxy, alkoxy or

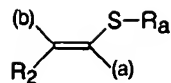
aryloxy group, or an amino group and/or a -COOH or COOM group, where M is a C1 to C3 alkyl; a phenyl or benzyl radical, in which the phenyl radical is optionally substituted by at least one C1 to C5 alkyl or alkoxy radical, these being optionally substituted by an amino group, or by a nitrogenous or oxygenous heterocycle, a -COOH or -COOM group; or a saturated -CH<sub>2</sub>-heterocycle group, with 5 or 6 elements, nitrogenous and/or oxygenous; R<sub>2</sub> represents a hydrogen atom, a C1 to C5 alkyl radical, or a -CH<sub>2</sub>-COO-alkyl (C1 to C5) group; and R<sub>3</sub> represents a hydrogen atom, a C1 to C5 alkyl or alkenyl radical, optionally substituted by -OH, a phosphate group, an alkoxy radical, in which the alkyl radical is C1 to C3, or an aryloxy radical; or an alkyl (or aryl), carbonyloxy group; or also R<sub>2</sub> and R<sub>3</sub> together form a ring with 5 or 6 carbon atoms; and R and R<sub>3</sub> can be linked to form a cycle of 5 to 7 atoms (carbon, oxygen, sulphur)

- α represents

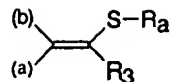
either a single bond, when A and A' represent A<sub>1</sub> and A<sub>1</sub>': or when A and A' represent A<sub>2</sub>, i.e. a -CHO or -COCH<sub>3</sub> group, and B<sub>2</sub> and B<sub>2</sub>' represent



or, when A and A' represent a -CHO group and B<sub>2</sub> and B<sub>2</sub>' represent R<sub>1</sub>, a group of formula



or a group of formula



in which (a) represents a bond towards  $\underline{Z}$  and (b) a bond towards the nitrogen atom.

-  $\underline{Z}$  represents a C6 to C21 alkylene radical, optionally with insertion of one or more multiple bonds, and/or one or more O and/or S heteroatoms, and/or one or more aromatic rings, and the pharmaceutically acceptable salts of these compounds.

<sup>22</sup>  
50. (New) Pharmaceutical compositions according to claim <sup>20</sup>~~48~~, in a form which may be administered by at least one of the oral route, injectable route, or rectal route.

<sup>23</sup>  
51. (New) A precursor according to claim <sup>1</sup>~~29~~ wherein said aryl radical is a phenyl radical.

<sup>24</sup>  
52. (New) A method according to claim <sup>21</sup>~~49~~ wherein said aryl radical is a phenyl radical.

<sup>25</sup>  
53. (New) A precursor according to claim <sup>1</sup>~~29~~ wherein said aryloxy is a phenoxy.

<sup>26</sup>  
54. (New) A method according to claim <sup>21</sup>~~49~~ wherein said aryloxy is a phenoxy.

<sup>27</sup>  
55. (New) A method according to claim <sup>21</sup>~~49~~ wherein said animal is a man.